reference. The Office Action also rejects Claims 18-22 under 35 U.S.C. § 103(a) as rendered unpatentable based upon three (3) separate references.

Rejection under 35 U.S.C. §112, second paragraph

Claims 18-22 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse.

In the rejection, the Office Action appears to object to the wording "which, when co-administered, suppress the formation of staphylococcal strains resistant to the lysostaphin, the cell-wall active antibiotic and combinations of lysostaphin and the cell-wall active antibiotic." There is nothing in this terminology that is indefinite.

The wording of the claims is clear and unambiguous. The individual species of staphylococcal strains need not be enumerated for the meaning of the claim to be apparent to one of ordinary skill in the art. Here the claim refers to staphylococcal strains that are delineated functionally. Functional language is a commonly accepted means of determining the scope of a claim and its meaning would be clear to one of ordinary skill in the art.

In a similar manner, Applicants point out that a correlation among the different parts of the claim does establish that a term in a claim is definite. The dosages called for in the claim are clear in that the claim calls for "an amount of lysostaphin independently effective in therapeutically treating a staphylococcal infection in a mammal" and "an amount of a cell-wall active antibiotic sufficient to treat, independently, a staphylococcal infection in a mammal." These dosages are clear regardless of the species of mammal or type of staphylococcal infection since a sufficient amount of both lysostaphin and cell-wall active antibiotic can easily be determined, and the function for each dosages is set forth in the claim. See M.P.E.P. 2173.05(c)(III). Accordingly, reconsideration and withdrawal is respectfully requested.

Rejection under 35 U.S.C. §102(b)

Claims 18-22 are rejected under 35 U.S.C. §102(b) as anticipated by Polak et al., (Diagn. Microbiol. Infect. Dis., (1993) vol.17, pp.265-270.

Applicants respectfully traverse.

The claimed invention is drawn, *inter alia*, to an *in vivo* method of treatment comprising combining an amount of lysostaphin independently effective in therapeutically treating a staphylococcal infection in a mammal with an amount of a cell-wall active antibiotic sufficient to treat, independently, a staphylococcal infection in a mammal.

Polak et al., does not describe an *in vivo* method. Polak et al. is limited to disclosing *in vitro* studies involving lysostaphin and another antibiotic in either broth or milk against limited strains of staphylococcus. There is no *in vivo* administration of lysostaphin or other antibiotic to a mammal as required to meet the claimed invention. In addition, none of the amounts of lysostaphin or other antibiotic used in the *in vitro* analysis of Polak et al. is predictive of the dosage amounts that would be required in an *in vivo* application of a combination therapy according to the invention. In fact, with respect to dosage amounts, Polak et al. fails to teach dosages according to the claimed invention.

In addition, Polak et al. is directed to the synergistic action of lysostaphin, *in vitro*, with another antibiotic. In each of the data tables 2-5, on pages 267-268 of Polak et al., demonstrates different levels of lysostaphin or the antibiotic that is utilized for the *in vitro* analysis. There is no teaching or suggestion throughout Polak et al. of combining an amount of lysostaphin independently effective in therapeutically treating a staphylococcal infection in a mammal with an amount of a cell-wall active antibiotic sufficient to treat, independently, a staphylococcal infection in a mammal. As such, Polak et al. fails to teach an *in vivo* method in dosage amounts that will meet the claim. Therefore, Polak et al. does not anticipate the

claimed invention.

Reconsideration and withdrawal are respectfully requested.

Rejection under 35 U.S.C. §103(a)

Claims 18-22 are rejected under 35 U.S.C. §103(a) as unpatentable based on Shaffner et al., Yale J. Biol. Med. (1967), vol. 39, no. 4, pp.215-219; Moreira et al., Antimicrobial Agents and Chemotherapy (Aug. 1997), vol. 41, no.8, pp.1788-93; or DeHart et al., Applied and Environmental Microbiol. (1995), vol. 4, pp.1475-1479.

Applicants respectfully traverse for the following reasons.

Shaffner et al., like Polak et al. above , is limited to *in vitro* studies. In addition, the Giorgio strains of Staphylococcus listed in Table 1, at page 224, referred to within the Office Action, is merely reported with respect to sensitivity to lysostaphin and penicillin. There is no teaching or suggestion throughout the reference that more than one antibiotic is utilized in a method of treatment. In fact, the reference teaches that certain variants of the Giorgio strain have high resistance to either lysostaphin or penicillin. One of ordinary skill in the art would not be motivated to include an antibiotic against which an organism has high resistance in a combined antibiotic treatment with another antibiotic against which that same organism has a lower resistance. So, if anything, Schaffner et al. teaches away from the claimed invention, and not toward it as the Office Action states.

Furthermore, Schaffner et al. fails to contemplate the problem in the art addressed in the instant invention. Applicants are the first to discover that bacteria can be resistant to either a cell-wall antibiotic, or lysostaphin, but not both. Schaffner et al. does not recognize this phenomena and accordingly, fails to provide motivation to combine these components in one method.

Moreira et al., like the previous references, fails to teach or suggest an *in vivo* method

and is limited to an *in vitro* study. In Moriera et al., certain Staphylococcus strains are evaluated for the effect of vancomycin and teicoplannin. In fact, lysostaphin is not even administered in any analytical run. As in Schaffner et al., the strains of organism have varying levels of lysostaphin resistance. Clearly Moriera et al., falls far from teaching Applicants' invention and, if anything, teaches away in that the strains are lysostaphin resistant. DeHart et al. is also an *in vitro* study of the intracellular mechanisms affected by the gene encoding lysostaphin. There is no teaching or suggestion of an *in vivo* method involving two separate antibiotics.

In addition, for the same reason that Schaffner et al. fails to contemplate the problem in the art addressed in the instant invention, the remaining references in this combination are also lacking. Applicants are the first to discover that bacteria can be resistant to either a cell-wall antibiotic, or lysostaphin, but not both. Schaffner et al. does not recognize this phenomena, and accordingly, fails to provide any motivation to combine these components in one method. Moriera et al. and DeHart et al. also fail to provide any motivation to combine these references based on the mutual resistivity of bacteria to either lysostaphin or a cell-wall antibiotic. Accordingly, Moriera et al. and DeHart et al. both fail to cure the deficiencies of Schaffner et al. on this point.

For all of the above reasons, the rejections should be withdrawn. Neither Schaffner et al., Moriera et al., or DeHart et al. teach or suggest all the elements of the invention. The simple *in vitro* study of different cellular mechanisms within each reference would not motivate one of ordinary skill in the art make the claimed invention.

Reconsideration and withdrawal of each obviousness rejection is respectfully requested.

Conclusion

Applicants assert that this application is now in condition for allowance and therefore request favorable consideration. If any issues remain to be addressed in this matter, which might be resolved by discussion, the Examiner is respectfully requested to call Applicants' undersigned counsel at the number indicated below.

Respectfully submitted,

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